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EXAMINER	
LIU, SAMUEL W	

ART UNIT	PAPER NUMBER
1656	

NOTIFICATION DATE	DELIVERY MODE
08/18/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/564,796	DEKKER ET AL.	
	Examiner	Art Unit	
	SAMUEL W. LIU	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/13/06 & 6/26/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *11-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/26/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of claims

Claims 1-20 are pending.

The response filed June 26, 2009 which presents claims 1-20 has been entered.

IDS

The references cited in the IDS filed 6/26/09 have been considered by Examiner.

Election/Restrictions

Applicants' election filed 6/26/09 of Group I, claims 1-10 with traverse is acknowledged. The traversal is on the grounds that Group II, claims 11-15, relates to a composition which is used in the elected Group I, claims 1-10; and thus, Group I and II should be a single invention (see 3rd paragraph, the "Remarks" filed 6/26/09). Applicants submit that the composition of Group II is not obvious in view of Weinbach et al. becasue the polylysine and protamine in the formulation taught by Weinbach et al. is synthetic and protamine (arginine-rich) in said formulation are isolated wherein the polylysine is synthetic, and becasue Weinbach et al. do not teach or suggest a peptide mixture obtained by hydrolysis of ordinary proteins (see the "Remark", paragraphs 3 and 4). The applicants' arguments are found unpersuasive because instant claims 11-15 as written do not require that the components of the claimed composition is made by a process (such as hydrolysis), but rather are directed to a composition comprising arginine-rich (the protamine) and lysine-rich (the polylysine) peptides/polypeptides of at least 20 w/w% arginine and lysine. Weinbach et al. teach the structural limitation of claim 11-15 above. Thus, Weinbach et al. show that Group II is not a contribution over the prior art and a holding of lack of unity is proper. Furthermore, applicant did not distinctly and specifically point out the

supposed errors between other groups as well. Therefore, the restriction requirement for claims 1-20 (Groups I-VIII) is still deemed proper and is therefore made FINAL.

Claims 11-20 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Therefore, claims 1-10 are under examination.

Objection to specification

At page 6, line 30, "IMAC" and "HP" should be spelled out in full for the first instance of use.

Objection to Claims

In claim 6, "a cut-off" should be changed to "a molecular weight cut-off" in order to be consistent with the immediately followed phrase "of 10 KDa".

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "20 w/w%"; the recitation is unclear whether or not the "w/w%" refers to a percent of total peptides or total amino acid weight, or/and a percent of total weight of total peptides or amino acids plus total weight of non-protein such as polynucleotides,

polysaccharides and lipids. The specification does not define the "protein content". The art (Josefina et al. (2005) "*Amino acid composition of some Mexican foods*", pages 1-12) teaches that "protein content" is not equal to amino acid composition (see p.6, the paragraph labeled "*Quiote*"), and teaches that the "protein content" refers to % of total proteins (by weight) in a composition such as food (by weight) (see p.6, the paragraph labeled ""Quiote"). Thus, the claimed "protein content" vaguely refers to a w/w% of amino acids (Lys and Arg) in a material comprising the peptides and **non-protein** molecules. This is because the specification defines the "protein source" as any protein-containing material, e.g., plant or animal materials (see p.9, lines 25-30); this indicates said "mixture of peptides" obtained from the "protein source" comprises the non-protein molecules, e.g., polynucleotides, lipids and polysaccharides. Thus, "based on the protein base" recited in claim1 *per se* does not clarify the basis of "w/w%" thereof. Claims 2-10 which depend from claim 1 are also rejected.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 7, and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Tomita et al. (US Pat. No. 5317084) wherein the ionic strength is evidenced by Wikipedia ("Ionic strength" (2009, updated) http://en.wikipedia.org/wiki/Ionic_strength, pages 1 and 2).

At patent claims 1-4, and Examples 1-3, Tomita et al. teach a process of preparing a peptide mixture containing lactoferricin (LFCIN) which is a Lys-rich/Arg-rich peptide consisting of amino acid sequence "Phe-Lys-Cys-Arg-Arg-Trp-Gln-Trp-Arg-Met-Lys-Lys-Leu-Gly-Ala-Pro-Ser-Ile-Thr-Cys-Val-Arg-Arg-Ala-Phe" (see patent claim 1), which contains 32% of Lys and Arg residues. Per each molecular weight of each amino acid in said sequence (see "*Amino acid MW attachment*"), Lys and Arg residues have molecular weight about 42.7 w/w% of total molecular weight of the entire peptide.

The process comprises (see patent claims 1 and 4) enzymatically hydrolysing bovine LFCIN (equivalent to instant claim 1, step a); contacting a mixture of peptide containing LFCIN with a cation-exchange column (equivalent to instant claim 1, step ***b***); rinsing the column with a buffer (patent claim 1, step b) wherein said buffer is a potassium phosphate buffer of alkaline pH 7.8 (patent claim 2) of molar concentration of 100 mM (see Example 2) (equivalent to instant claim 1, step ***c***); and desorbing (i.e., eluting) the peptide from the column with a solution containing a salt at a concentration of 1 to 4 M at pH 7-8 (see patent claim 1, step c) (equivalent to instant claim 1, step ***d***), wherein the salt concentration "1 to 4 M" falls into the limitation "normality of 0.05-2.0" set forth in instant step d). Thus, Tomita et al. teach claims 1, 3, 4 and 10

Tomita et al. teach equilibrating the column with 100 mM KH_2PO_4-K_2HPO_4 buffer, pH7.8. The ionic strength (I) calculation is the following.

$I = ½ [(0.1 \times 2 \times 1^2) + (0.1 \times 2^2) + (0.033 \times 2^2) + (0.033 \times 1^2)] = 0.76$, wherein, for 100 mM, the concentration of the ions of K_2HPO_4 are $[K^+] = 0.1 \times 2$ and $[HPO_4^-] = 0.1 \times 2^2$; and the concentration of the ions of KH_2PO_4 are $[K^+] = 0.1 \times 2$ and $[HPO_4^-] = 0.33$. The calculation is in

accordance with Wikipedia (2009, updated) "Ionic strength". This meets the limitation of claim 2.

Since in the process above, the starting material is the "peptide mixture" which must contain more than one peptide, Tomita et al. also teach claim 7.

Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

[1] Claims 1, 5, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tomita et al. (US Pat. No. 5317084) as applied to claim 1 above, and in view of DeFrees et al. (US 2008/027487 A1).

The teaching of claim 1 by Tomita et al. has been set forth above.

Yet, Tomita et al, do not expressly teach filtration of the enzymatically digested sample containing the peptide which is preceded by applying the sample to the column.

DeFrees et al. teach removal of degradative enzymes by filtration prior to the cation exchange chromatographic step (see [0027], lines 3-7), and teach use of filtration membrane of molecular weight cut-off (MWCO) to carry out said filtration step prior to chromatographic purification (see [0192], lines 4-9), wherein MWCO range about 5-200 KDa depending peptide of interest (see [0192], lines 14-17), as applied to claims 5 and 6.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to perform the filtration prior to purification by the column using a proper MWCO membrane in the process of preparing a peptide mixture containing lactoferricin above. This is because the filtration is known in the art (see [0185], line 1, DeFrees et al.) at the time the instant invention was made, and because, in addition to this, the primary reference has also taught use of filtration technique for isolating the lactoferricin peptide despite stepwise difference, i.e., the use is in the last step thereof (see col. 5,lines 23-29, Tomita et al.). Further, the filtration, e.g., tangential flow filtration (TFF) taught by DeFrees et al. offers advantages: (i) not only removal of the proteolytic enzymes but also removal of cellular debris when the peptide mixture is prepared from a cellular source (see [0027], lines 3-5, and [0112]), and (ii) allows for semi-purification of the peptide of interest and allows the peptide to be concentrated (see [0195], line 14) by separating small peptides from larger contaminants (see [0193]). Upon reading the DeFrees' reference, one of ordinary skill in the art of peptide purification would haverealized/appreciated these advantage, and would have readily tried to choose proper size (MWCO) of the filtration membrane such as MWCO10 for separating the lactoferricin above based on the teaching on paragraphs [0191]-[0195], e.g., the membranes have a MWCO selected according to the size of the peptide being isolated (see [0192, lines 12-16, DeFrees et al.).

Determining the proper MWCO for separating the peptide is thus considered to be prima facie obvious in the absence of any unexpected result. Therefore, combination of the references' teachings renders claims 5 and 6 prima facie obvious.

[2] Claims 1, 8, and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tomita et al. (US Pat. No. 5317084) as applied to claim 1 above, and in view of Jensen et al. (US 2007/0104764 A1).

The teaching of claim 1 by Tomita et al. has been set forth above.

Yet, Tomita et al, do not expressly teach the protein source for the lactoferricin is a vegetable origin.

Jensen et al. teach recombinant expression/production of antimicrobial peptide (see [0016], line 3) including the lactoferricin peptide (see abstract, line 5, and [0052], [0054]-[0055]) from a plant host, e.g., pea, cotton or soybean (see [0215], and [0217], lines 9 and 10), as applied to claims 8 and 9.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to recombinantly producing the lactoferricin peptides from the vegetable plant such as soybean, pea or cotton for preparing the lactoferricin peptide mixture. This is becasue the expression in the plant cells can result in recoverable quantities, and improved quality of feed as well as improved nutritional value (see [0215], Jensen et al.), and because said expression can also improve production economy (see [0012], Jensen et al.). Thus, one of ordinary skill in plant biologist would have been motivated by the reference teaching to try using plant cell such as pea cells to express/produce the desired lactoferricin peptides. When tried so, it would have been led

to reasonable expectation of success. Therefore, combination of the references' teachings renders claims 8 and 9 *prima facie* obvious.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:30 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

/Samuel Wei Liu/
Patent Examiner, Art Unit 1656

/ANAND U DESAI/
Primary Examiner, Art Unit 1656
August 13, 2009